ACUTE MYELOID LEUKEMIA WITH T-LYMPHOID EXPRESSION AND DISTINCT CHROMOSOMAL ABNORMALITIES

To the Editor:

The report by Cuneo et al. on adult acute myeloid leukemia (AML) expressing lymphoid markers illustrates an interesting clinicopathologic problem that we have recently encountered. A 20-year-old man presented with bilateral tonsillar enlargement and lymphadenopathy in the cervical, axillary, and inguinal regions. Full blood count was: hemoglobin 88 g/L, white blood cell count 57 x 10^9/L, platelets 69 x 10^9/L. The bone marrow was hypercellular with 93% blasts, some with coarse granules but no Auer rods. Sudan Black was faintly positive in 3% of the blasts. A working diagnosis of AML (French-American-British [FAB]-M1) was made and the patient was randomized in the DAT 3 + 10 arm of the Medical Research Council (MRC) AML10 trial protocol. Subsequently immunophenotyping from two different laboratories gave the results summarized (Table 1).

These results were discrepant for the following reasons. First, cytoplasmic CD3 reactivity was negative in one laboratory. Secondly, Tdt reactivity was ambiguous from one laboratory but definitive from the other. Lastly, TCR 8y gene rearrangement was positive in one laboratory and not tested in the other. Thus, both laboratories showed coexpression of myeloid and T-lymphoid markers but emphasis was subtly different, one tending toward a lymphoid and the other toward a myeloid interpretation. Cytogenetic analysis of the marrow leukemic cells showed hyperploidy in 19 of 30 cells examined (1 cell 47XY, +19, 18 cells 49XY, +7, +19, +21) with no structural abnormalities.

The important issue about these results is that they had no bearing on the intention to treat as a case of AML. The decision was taken purely on morphologic and cytochemical grounds and the patient achieved complete remission after one course of chemotherapy. The cytogenetic abnormalities in our case do not fit any of the four chromosomally distinct subgroups from the 34 cases analyzed by Cuneo et al.; in addition, trisomy 7 is exceptionally rare in myeloid diseases. This case highlights the need for further similar studies of the relationship between morphologic, immunologic, and cytogenetic (MIC) classifications, with the ultimate aim of giving specific treatment for different subgroups.

Currently, the decision to treat such patients must still be made on morphologic and cytochemical (FAB) criteria. The current MIC proposal for reclassification of acute leukemia does not yet address this problem. We believe that the response in therapy in these patients with transitional forms between AML and T-acute lymphoblastic leukemia should be reviewed to analyze whether such aberrant features influence responsiveness to various protocols.

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RESPONSE

In our report published in Blood earlier this year,1 cytogenetic data were studied in 34 patients with unequivocal acute myeloid leukemia (AML) by French-American-British criteria in which lymphoid markers (LM) were detected by immunophenotypic and genetic analysis. Six patients had i1q23 rearrangements, 3 had the Ph chromosome, 15 had aberrations of the "myeloid type," and 10 had a normal karyotype. In agreement with our findings, no patient with hyperdiploid karyotype or other aberrations usually associated with lymphoid leukemias was found in a literature review of 54 cases of adult AML with LM.

Chan-Lam et al describe a case of acute leukemia classified as myeloid on a cytologic basis, showing a hyperdiploid karyotype, in which several T-cell features were present. This patient does not fit any of the chromosomal groups of AML with LM identified in our study; the following considerations, however, may account fairly well for this discrepancy.

The patient described by Chan-Lam et al cytologically does not have unequivocal AML and does not fulfill the inclusion criteria adopted in our study. Scattered azurophilic granules can be observed in primitive cells in acute lymphoblastic leukemia (ALL),2 and sudan black-B positivity was previously detected in 6 of 350 (1.6%) well-documented cases of ALL.3 These leukemias can be shown to be lymphoblastic in nature by negativity for the myeloperoxidase stain that appears to be more specific for the granulocytic lineage. Ultrastructural studies now have an established role in lineage assignment in doubtful cases.4

This patient presented with lymph node enlargement, a feature extremely uncommon in myeloblastic leukemia, except in the monocytic variant5 and shows TCR rearrangement as well as CD2 and CD7 positivity. The demonstration of acid phosphatase and acid a-naphthyl acetate esterase activity has been recommended for a correct cytologic diagnosis of T-cell ALL.6

Thus, we agree that the classification of acute leukemia must be firmly established on morphologic and cytochemical basis and treatment chosen accordingly. Cytologic classification can be integrated with immunologic and cytogenetic findings to better delineate some disease subsets of acute leukemia with distinct clinicopathologic features and prognosis. With regard to AML with LM, the suggestion can be drawn from morphologic, immunologic, and cytogenetic studies that patients with specific chromosome abnormalities (i1q23 rearrangements, Ph chromosome) and with extensive lineage infidelity may have lower complete remission rate than patients with favorable cytogenetic abnormalities or with normal karyotype.

Therefore, it is not surprising that a patient with a hyperdiploid karyotype, a feature commonly regarded as a favorable prognostic indicator in ALL, may achieve complete remission after chemotherapy using anthracyclines and cytarabine, both drugs being effective on myeloid blasts and on lymphoid blasts.

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